AMENDMENTS

IN THE CLAIMS:

Please amend the following claims:

1. (Twice amended) A method for detecting tumor-derived or tumor-associated RNA in the plasma or serum fraction of blood from a human or animal, wherein the tumor-derived or tumor-associated RNA is epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of:

   a) extracting ~~mammalian~~ total RNA from plasma or serum from a human or animal, wherein a fraction of said extracted RNA comprises a tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

   b) amplifying or signal amplifying said fraction of the extracted RNA or corresponding cDNA prepared therefrom, wherein amplification is performed either qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

   c) detecting the amplified product produced from the RNA or cDNA.

2. (Twice amended) A method for detecting extracellular tumor-derived or tumor-associated RNA in a non-cellular fraction of a bodily fluid from a human or animal, wherein the tumor-derived or tumor-associated RNA is epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of:

   a) extracting ~~mammalian~~ total RNA from a non-cellular fraction of a bodily

fluid from a human or animal, wherein a fraction of said extracted RNA comprises an extracellular tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or cDNA corresponding thereto, wherein amplification is performed either qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from the RNA or cDNA corresponding thereto.

3. (Amended) The method of claim 1, wherein the amplification in step (b) is performed by a RNA amplification method that ~~amplifies the RNA directly or wherein the RNA is first reverse transcribed to cDNA whereby the cDNA is amplified, and wherein the amplification method~~ is reverse transcriptase polymerase chain reaction, ligase chain reaction, branched DNA signal amplification, amplifiable RNA reporters, Q-beta replication, transcription-based amplification, isothermal nucleic acid sequence-based amplification, self-sustained sequence replication assay, boomerang DNA amplification, strand displacement activation, or cycling probe technology.

4. (Amended) The method of claim 2, wherein the amplification in step (b) is performed by a RNA amplification method that ~~amplifies the RNA directly or wherein the RNA is first reverse transcribed to cDNA whereby the cDNA is amplified, and wherein the amplification method~~ is reverse transcriptase polymerase chain reaction, ligase chain reaction, branched DNA signal amplification, amplifiable RNA reporters, Q-beta replication, transcription-based

amplification, isothermal nucleic acid sequence-based amplification, self-sustained sequence replication assay, boomerang DNA amplification, strand displacement activation, or cycling probe technology.

5. (Amended) The method of claim 1, wherein detection of the amplified product in step (c) is performed using a detection method that is gel electrophoresis, capillary electrophoresis, Southern blot analysis, Northern blot analysis, reverse blot detection, high-performance liquid chromatography, or enzyme-linked immunosorbent assay (ELISA) ~~detection including~~ using biotinylated or other modified primers, labeled fluorescent or chromagenic probes, or laser-induced fluorescence detection ~~Southern blot analysis, Northern blot analysis, electroluminescence, reverse blot detection, or high-performance liquid chromatography~~.

6. (Amended) The method of claim 2, wherein detection of the amplified product in step (c) is performed using a detection method that is gel electrophoresis, capillary electrophoresis, Southern blot analysis, Northern blot analysis, reverse blot detection, high-performance liquid chromatography, or enzyme-linked immunosorbent assay (ELISA) ~~detection including~~ using biotinylated or other modified primers, labeled fluorescent or chromagenic probes, or laser-induced fluorescence detection ~~Southern blot analysis, Northern blot analysis, electroluminescence, reverse blot detection, or high-performance liquid chromatography~~.

9. (Twice amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of performing the method of claim 1 ~~qualitatively or quantitatively, and detecting~~

~~a product produced by said RNA in the plasma or serum of said animal or human,~~ wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

10. (Twice amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of performing the method of claim 1 ~~qualitatively or quantitatively, and detecting a product produced by said RNA in the plasma or serum of said animal or human,~~ wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

11. (Amended) A method according to claim 9 wherein the animal is a human.

12. (Amended) A method according to claim 10 wherein the animal is a human.

21. (Amended) A method for monitoring an animal or human for a malignant or premalignant disease, wherein the malignant or premalignant disease is associated with a tumor-derived or tumor-associated RNA that is epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, the method comprising the step of:

a) extracting ~~mammalian~~ total RNA from plasma or serum from a human or animal, wherein a fraction of said extracted RNA comprises epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or

corresponding cDNA, wherein amplification is performed qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto, to produce an amplified product; and

c) detecting the amplified product produced from RNA or cDNA corresponding thereto.

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37. (Twice amended) A method according to claim 1, further comprising the step of performing a diagnostic test for diagnosing cancer or premalignancy when epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof is detected in plasma or serum of an animal or human.

40. (Amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 ~~on~~ using blood plasma or serum from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

41. (Twice amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 ~~on~~ using an acellular fraction of a bodily fluid ~~blood or serum~~ from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

52. (Twice amended) A method for producing cDNA by reverse transcription of a fraction of extracellular ~~mammalian~~ total RNA extracted from plasma or serum from a human or animal, wherein the fraction comprises epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, whereby cDNA corresponding to said RNA is produced.

53. (Twice amended) A method for producing cDNA by reverse transcription of a fraction of extracellular ~~mammalian~~ total RNA extracted from an acellular fraction of a bodily fluid from a human or animal, wherein the fraction comprising epidermal growth factor RNA, epidermal growth factor receptor ~~(erb-B-1)~~ RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, whereby cDNA corresponding to said RNA is produced.

Please cancel claims 46 and 51 without prejudice or disclaimer.

REMARKS

Applicant wishes to thank the Examiner for the courtesies extended to his representative in the informal telephone interview, and for the Examiner's helpful comments and suggestions.

Applicant notes that his previous response contained a typographical error, and that claims 11 and 12 were inadvertently cancelled. Likewise, Applicant notes that the previous Office Action included claims 46 and 51, which claims the Examiner informed Applicant's representative should not be pending.

Applicant has cancelled claims 46 and 51, consistent with the Restriction Requirement mailed August 7, 2002. Applicant has also corrected the deficiencies noted in the previous Office Action for originally-filed claims 11 and 12, and requests that these claims be considered on the merits.